

· 综述 ·

急性冠脉综合征患者经皮冠状动脉介入治疗术后 对比剂肾病的防治进展

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【摘要】 经皮冠状动脉介入治疗是急性冠脉综合征的主要治疗措施。对比剂肾病是经皮冠状动脉介入治疗术后常见并发症之一。对于对比剂肾病缺乏有效治疗措施。术前做好对比剂肾病高危因素评估, 识别高危患者, 围手术期水化是最为有效的防治措施。另外, 他汀类药物和 N-乙酰半胱氨酸是研究最多的药物。现对急性冠脉综合征患者经皮冠状动脉介入治疗术后对比剂肾病防治进展进行综述。

【关键词】 对比剂肾病; 急性冠脉综合征; 经皮冠状动脉介入治疗; 防治

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Prevention of Contrast Induced Nephropathy after Percutaneous Coronary Intervention in Patients with Acute Coronary Syndrome

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【Abstract】 Percutaneous coronary intervention has been the main treatment for acute coronary syndrome. Contrast induced nephropathy (CIN) is one of the common complications after percutaneous coronary intervention. There are no effective treatment for CIN. Preoperative assessment of risk factors before emergency percutaneous coronary intervention, identification of high-risk patients, and perioperative adequately hydration are the most effective measures for prevention of CIN. In addition, statins and N-acetylcysteine have been the most extensively studied drugs. This article reviews the progress in the prevention of contrast induced nephropathy after percutaneous coronary intervention in patients with acute coronary syndrome.

【Key words】 Contrast induced nephropathy; Acute coronary syndrome; Percutaneous coronary intervention; Prevention

经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 是急性冠脉综合征 (acute coronary syndrome, ACS) 患者的首选治疗措施, 对比剂广泛应用于 PCI 术中, PCI 术中应用对比剂后出现的急性肾损伤 (acute kidney injury, AKI) 称作对比剂诱导的急性肾损伤 (contrast-induced acute kidney injury, CI-AKI) 或对比剂相关的急性肾损伤 (contrast associated acute kidney injury, CAAKI) 或对比剂肾病 (contrast induced nephropathy, CIN), 是 ACS 患者常见的并发症, 增加远期死亡率, 是不良预后指标^[1]。临床上 CIN 的早期定义为在排除肾毒性药物、缺血性肾病等因素

影响后, 血管内注射对比剂后肌酐 48 h 内较基线增加 25% 或 ≥ 0.5 mg/dL ($44 \mu\text{mol/L}$)^[2]。2012 年改善全球肾脏病预后组织 (KDIGO) 将其定义为血管内注射对比剂后 72 h 内肌酐较基线增加 ≥ 0.3 mg/dL ($26.5 \mu\text{mol/L}$), 或 1 周内增加 50% 以上, 或持续 6 h 以上尿量 < 0.5 mL/(kg·h)^[3]。多数患者为一过性肌酐升高, 3~5 d 肌酐达峰值, 7~10 d 恢复到基线水平^[2], 但是对于高危患者仍可能出现持续性肾功能不全。CI-AKI 的发生显著增加 ACS 患者死亡率及主要不良心脑血管事件, 是患者远期不良预后的独立预测因素^[4-5]。目前对 ACS 患者 CIN 的防治是以生理盐水

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水化为主的支持治疗,尚无有效治疗措施,现从术前风险评估、水化治疗、他汀类药物、N-乙酰半胱氨酸、对比剂应用、肾脏替代治疗等方面对 ACS 患者 PCI 术后 CIN 的防治进行综述。

1 术前风险评估

ACS 患者 PCI 术后 CIN 的危险因素包括肾功能不全、糖尿病、高血压、高龄、心力衰竭、对比剂剂量 > 200 mL、心源性休克、肾毒性药物应用、贫血、低蛋白血症、主动脉内球囊反搏的使用^[6-9],慢性肾脏病是最重要的危险因素,慢性肾脏病患者多合并高血压、糖尿病,死亡风险更高^[1]。高尿酸血症也是 CIN 发生的重要危险因素^[10]。

Mehran 评分包括低血压、应用主动脉内球囊反搏、充血性心力衰竭、年龄 ≥ 75 岁、贫血、糖尿病、对比剂应用 > 100 mL、肌酐基础值 > 1.5 mg/dL (132 $\mu\text{mol/L}$)、估算肾小球滤过率 (estimated glomerular filtration rate, eGFR) < 20 mL/(min $\cdot 1.73 \text{ m}^2$) 或 20 mL/(min $\cdot 1.73 \text{ m}^2$) \leq eGFR ≤ 40 mL/(min $\cdot 1.73 \text{ m}^2$) 或 40 mL/(min $\cdot 1.73 \text{ m}^2$) < eGFR ≤ 60 mL/(min $\cdot 1.73 \text{ m}^2$) 等指标,评分越高,急性心肌梗死患者术后 CIN 风险及出现持续肾功能不全和远期临床结局的风险越高^[11]。Mehran 评分包括术中对对比剂剂量指标,术前难以完成详细评估,而由高龄、左室射血分数下降、肾小球滤过率下降组成的 AGEF 评分能预测 ST 段抬高心肌梗死 (ST segment elevation myocardial infarction, STEMI) 患者急诊 PCI 术后 CIN 发生 (OR = 5.19, $P < 0.001$, AUC = 0.88)^[12]。由心率 > 100 次/min、收缩压 < 100 mm Hg (1 mm Hg = 0.133 3 kPa)、年龄 ≥ 75 岁和 Killip > 1 四项指标组成的 C-ACS 评分系统对 STEMI 患者 PCI 术后 CIN 及临床预后有良好的预测价值^[13]。CHA₂DS₂-VASc 评分可预测 ACS 患者 PCI 术后 CIN 的发生 (AUC = 0.769, 95% CI 0.733 ~ 0.805, $P < 0.001$), CHA₂DS₂-VASc 评分 ≥ 4 分是 CIN 发生率的独立预测因素^[14]。另外术中罪犯血管 Syntax 评分 > 10 分,是 STEMI 患者急诊 PCI 术后发生 CI-AKI 的重要决定因素^[15]。对于拟行急诊 PCI 的患者,这些评分系统可能更有利于对 CIN 风险做出初步评估。

2 水化

水化治疗能增加肾血流量、稀释对比剂,是预防 PCI 术后 CIN 的重要措施,口服和静脉补液进行水化均可有效减少 CIN 的发生^[16]。一项包括 3 项随机对照研究纳入 924 例行急诊 PCI 的 STEMI 患者的荟萃分析^[17]显示,围手术期生理盐水水化可显著降低 CIN 发生率 (水化组 16.9% vs 对照组 26.4%, $RR = 0.64$, 95% CI 0.50 ~ 0.82, $P = 0.0005$),但并不减少

术后肾脏替代治疗需要和死亡率。另一项纳入 1 074 例行急诊 PCI 的 STEMI 患者的荟萃分析^[18]表明,和未水化的对照组比较,急诊 PCI 时静脉水化对 CIN 发生率降低 42% ($RR = 0.58$, 95% CI 0.45 ~ 0.74, $P < 0.001$)。对于行急诊 PCI 的 ACS 患者,常合并存在心力衰竭、容量负荷不足、低血压等情况,补液水化是最重要的治疗措施。近期 Liu 等^[19]对 560 例 STEMI 患者的多中心随机对照研究表明,根据左心室舒张末压积极水化,CI-AKI 发生率较常规水化更低 (21.8% vs 31.1%),两组急性心力衰竭的发生率并无显著差异,积极水化在 CI-AKI 防治上有更好的疗效,尤其是对于肾功能不全、非左前降支病变的急性心肌梗死患者。ACS 患者是 CIN 高危人群,术前开始水化治疗是安全有效的预防措施。

水化晶体的选择临床上主要以生理盐水为主,而碳酸氢钠的碱化作用,可以中和氧自由基的肾损伤作用,既往有研究显示碳酸氢钠水化可减少 CIN 的发生。CINSTEMI 研究^[20]是对 720 例行急诊 PCI 的 STEMI 患者的随机对照研究,相对于生理盐水 ($n = 181$),碳酸氢钠 ($n = 181$) 水化可以减少 CIN 的发生,但二者无统计学差异 (20.1% vs 26.5%, $P = 0.43$)。PRESERVE 研究^[21]中对行 PCI 的合并慢性肾脏病的稳定型冠心病的亚组分析,其中 2 511 例行碳酸氢钠水化,2 482 例行生理盐水水化,两组 CAAKI 发生率并无显著差异 (4.4% vs 4.7%, $P = 0.62$)。相对于生理盐水,碳酸氢钠水化在 ACS 患者 CIN 的防治上并无优势,目前指南对于 CIN 的防治,推荐足够的生理盐水水化治疗作为基础治疗,尤其是对于肾功能不全的高危患者,建议术前术后生理盐水水化,术前 12 h 开始 1 mL/(kg \cdot h) 水化,术后持续 24 h,对于左室射血分数 $\leq 35\%$ 或心功能 (NYHA 分级) > 2 级者,可予以 0.5 mL/(kg \cdot h) 水化^[22-23]。

3 他汀类药物

关于他汀类药物在 CIN 中的应用,多为 PCI 术前高剂量负荷应用,他汀类药物对 ACS 患者有着明确的心血管保护作用,其对 CIN 防治上的具体机制不详。对 9 项临床随机对照试验 ($n = 5 212$) 的荟萃分析^[24]显示,术前短期强化他汀类药物治疗可显著降低 ACS 患者 CI-AKI 的风险 ($RR = 0.37$, 95% CI 0.25 ~ 0.55, $P < 0.0001$),而对非 ACS 患者的相关风险并无显著降低趋势 ($RR = 0.65$, 95% CI 0.41 ~ 1.03, $P = 0.07$)。ACS 患者 PCI 术前短期高剂量瑞舒伐他汀可减少 CI-AKI 发生,他汀类药物的肾脏保护可能与抗炎作用相关^[25]。中国一项纳入 496 例 ACS 患者的前瞻性随机对照研究^[26]显示术前高剂量阿托伐他汀可显著降低

ACS 患者 CIN 发生率 (6.4% vs 12.6%, $P = 0.02$)。然而美国一项纳入 2 055 例患者的观察性临床研究^[27]显示术前他汀类药物应用并不减少 ACS 患者在内的冠心病患者 PCI 术后 CI-AKI 的发生。尽管他汀类药物对 ACS 患者有一定的肾脏保护作用,目前具体保护机制仍不明确,可能与其心血管保护作用相关,2022 年加拿大放射学会指南^[28]不推荐他汀类药物作为 CI-AKI 的常规预防策略。鉴于其抗炎、抗氧化、调脂、稳定斑块等作用,可考虑对 ACS 患者术前短期高剂量他汀类药物治疗。

4 N-乙酰半胱氨酸

N-乙酰半胱氨酸能清除氧自由基、减轻术后氧化应激、减低对比剂的肾毒性,曾被认为是 CIN 防治的重要药物。然而另一项纳入 7 项临床对照研究的 meta 分析^[29] ($n = 1\ 710$) 指出,和未使用 N-乙酰半胱氨酸的对照组比较,对行急诊 PCI 的 STEMI 患者应用 N-乙酰半胱氨酸可显著降低 CA-AKI 的发生风险。2016 年一项纳入 43 项随机对照研究 ($n = 3\ 277$) 的荟萃分析^[30]指出,ACS 亚组中 N-乙酰半胱氨酸应用使 CI-AKI 发生率有下降趋势,但组间差异无统计学意义 ($OR = 0.758, 95\% CI 0.538 \sim 1.066, I^2 = 38.56\%, P = 0.111$),而非 ACS 亚组分析 N-乙酰半胱氨酸应用可显著减少 CI-AKI 发生 ($OR = 0.642, 95\% CI 0.492 \sim 0.838, I^2 = 33.73\%, P = 0.001$)。Garcia 等^[31]进行的 PRESERVE 研究是一项大样本的临床随机对照研究,对行 PCI 术的 1 161 例患者的亚组分析表明,N-乙酰半胱氨酸并不能降低合并慢性肾脏病的高危稳定型冠心病患者 PCI 术后 CA-AKI 发生风险。关于 N-乙酰半胱氨酸在 CIN 防治中的作用,多项临床研究结果差异较大,近来 Huang 等^[32]对 6 项临床研究 ($n = 199$) 进行的荟萃分析表明 N-乙酰半胱氨酸可使肌酐水平下降,而对胱抑素 C 无影响,肌酐检测并不能真实反映肾功能,可能无法对 CIN 做出准确诊断。因此 2022 年加拿大 CIN 防治指南^[23]不推荐使用 N-乙酰半胱氨酸防治 CIN。

5 对比剂应用

高渗对比剂发生 CIN 的风险高于等渗对比剂和次高渗对比剂,离子型对比剂发生 CIN 的风险高于非离子型对比剂。有临床随机对照研究^[33]显示 STEMI 急诊 PCI 术中使用次高渗对比剂出现 CI-AKI 的风险与等渗对比剂并无差异。荟萃分析^[34]结果表明不同的次高渗对比剂之间发生 CIN 的风险并无显著差异。近期美国一项纳入 536 013 例患者的回顾性临床研究^[35]表明,应用等渗对比剂发生不良肾脏和心血管事件的风险较次高渗对比剂低,尤其是在慢性肾脏病、

糖尿病和慢性冠状动脉闭塞患者中有明显差异。然而另一项包括 50 389 例患者的荟萃分析^[36]显示等渗对比剂和次高渗对比剂在 ACS 亚组中 CI-AKI 发生率无统计学差异。目前指南^[22,28]建议使用非离子型次高渗或等渗对比剂降低 CIN 风险,并不推荐优先使用等渗对比剂以降低 CIN 发生风险。关于等渗对比剂和次高渗对比剂发生 CI-AKI 风险是否不同,以及不同的次高渗对比剂或等渗对比剂之间发生 CIN 的风险是否存在差异并不明确。

使用更高剂量的对比剂与 CIN 发生率及死亡率增加相关,临床上应尽可能选择满足诊疗需求的最低剂量。有研究^[37]支持以 $5 \times$ 体重 (kg)/基线肌酐 (mg/dL) 作为术中对比剂应用的最大可接受剂量。对比剂剂量与基线 eGFR 比值 (CV/eGFR) 是 CIN 发生的重要预测因素,一项对 470 例行急诊 PCI 术的 STEMI 患者的临床研究^[38]显示应用 CV/eGFR 预测 CI-AKI 优势明显,其比值 < 2.5 时可显著降低 CI-AKI 发生风险。Kurogi 等^[39]对 952 例 AMI 患者的观察性研究显示 CV/eGFR > 3.45 是急诊 PCI 术后发生持续肾功能不全的重要预测指标,PCI 术中对比剂的使用需充分考虑患者肾功能,2018 年欧洲心肌血运重建指南^[22]建议使用术中 CV/eGFR < 3.7 。

6 肾脏替代治疗

对于慢性肾脏病患者行血液透析可以加速对比剂的排泄,但由于导管的放置和感染相关风险,CIN 患者存在肾功能进一步恶化的风险。ACS 患者合并严重肾功能不全和心力衰竭时,PCI 术后积极血液透析可能对患者生存率有所改善^[40],一项纳入 1 010 例患者的荟萃分析^[41]显示对于合并慢性肾脏病的择期 PCI 的患者,肾脏替代治疗并不降低 CIN 的发生风险。2020 年一项回顾性研究^[42]显示大流量间歇性血液透析可能减少严重慢性肾脏病患者 PCI 后 CIN 的发生。肾脏替代治疗对 ACS 患者 CIN 防治研究相对较少,由于有创性及出血风险高,需要进一步研究评估特定的最大受益人群,2021 ACC/AHA/SCAI 血运重建指南不推荐肾脏替代治疗作为降低 CI-AKI 风险的预防措施^[23]。

7 其他防治措施

粥样硬化性栓塞可能与 AKI 发生相关,经股动脉介入路径临近肾动脉,可能会增加 AKI 发生风险,近期一项纳入 46 816 例患者的 meta 分析^[43]表明选择经桡动脉路径可降低 PCI 术后 AKI 风险 ($OR = 0.66, 95\% CI 0.54 \sim 0.81, P < 0.000\ 1, I^2 = 74\%$)。小样本单中心随机对照研究显示缺血后适应^[44]、远端缺血预适应^[45]可降低 ACS 患者 PCI 术后 CIN 的发生率,目

前其在 CIN 预防中的作用尚不确定,需要大规模的临床研究进一步探索。

8 总结

CIN 是 ACS 患者 PCI 术后的常见并发症,增加术后主要不良心血管事件发生率,目前尚无有效治疗措施,做好术前风险评估、使用肾毒性小的等渗或次高渗对比剂、尽可能减少对对比剂使用剂量、PCI 围手术期充分水化是有效防治策略,对于 ACS 患者不应因 CIN 发生风险高而延迟行血运重建治疗。

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更正

《心血管病学进展》2021 年第 42 卷第 6 期 488 页已发表的文章《机器学习 CNN 模型在心血管疾病诊疗中的临床应用及研究进展》的第一作者艾克力亚尔·艾尼瓦尔的单位名称由“新疆医科大学研究生院, 新疆乌鲁木齐 830054; Xinjiang Medical University Graduate School, Urumqi 830054, Xinjiang, China”更正为“新疆医科大学第一医院, 新疆乌鲁木齐 830054; The First Affiliated Hospital of Xinjiang Medical University, Urumqi 830054, Xinjiang, China”, 特此证明。

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